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Research Progress on Hydrogen-Rich Water in Improving Ocular Surface Diseases and Oxidative Stress

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Abstract: The occurrence and development of ocular surface diseases are closely related to oxidative stress. Excessive accumulation of reactive oxygen species (ROS) can lead to ocular surface cell damage and inflammatory responses. As a new type of antioxidant, hydrogen-rich water (HRW) has shown intervention potential in ocular surface diseases such as dry eye and conjunctivitis by selectively scavenging toxic ROS, inhibiting inflammatory pathways, and protecting ocular surface cells. Combining basic mechanisms and clinical evidence, this article explores the application value of hydrogen-rich water in ocular surface diseases, providing new ideas for the prevention and treatment of oxidative stress-related eye diseases.

Keywords: Hydrogen-rich water; Ocular surface diseases; Fatigue relief

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1. Introduction

Ocular surface diseases are a group of common disorders that affect the structure and function of the ocular surface, including dry eye, allergic conjunctivitis, infectious keratitis, etc. Their incidence has been on the rise with the increase in age and the popularization of electronic devices [1]. Studies have shown that oxidative stress is one of the core mechanisms underlying the occurrence of ocular surface diseases: factors such as prolonged eye use, ultraviolet exposure, and inflammatory factors can induce ocular surface tissues (e.g., conjunctiva, cornea, lacrimal gland) to produce excessive ROS, which exceeds the scavenging capacity of the endogenous antioxidant system. This further trigger lipid peroxidation, protein damage, and DNA mutation, ultimately leading to apoptosis and functional impairment of ocular surface cells [2]. Hydrogen molecule (H_2), as a selective antioxidant, has demonstrated therapeutic advantages in various oxidative stress-related disease since it was discovered in 2007 that it can specifically scavenge hydroxy radicals (·OH) and peroxynitrite ($ONOO^-$) [3]. Hydrogen-rich water (HRW), which is rich in hydrogen molecules, possesses antioxidant, anti-inflammatory, and cell-protective properties. Its application in ocular surface diseases has gradually become a research focus. This article will discuss the association between oxidative stress and ocular surface diseases, the mechanism of action of HRW, and relevant clinical evidence.

2. Pathological association between oxidative stress and ocular surface diseases

2.1. Dry eye disease and oxidative stress

Dry eye disease is the most common ocular surface disorder, characterized by insufficient tear secretion or abnormal tear quality, which leads to damage of the ocular surface mucosa. Studies have shown that the level of reactive oxygen species (ROS) in the tears of patients with dry eye disease is significantly increased, and it is positively correlated with the severity of the disease [4]. ROS can exacerbate dry eye symptoms through the following pathways

2.2. Impairing tear film stability

Oxidative stress damages the acinar cells of the lacrimal gland, reducing the secretion of mucin and aqueous fluid. At the same time, it promotes the peroxidation of the lipid layer of the tear film, accelerating tear evaporation [5].

2.3. Inducing ocular surface inflammation

ROS activates the nuclear factor κB (NF-κB) pathway, promoting the release of inflammatory factors such as tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6), which triggers conjunctival hyperemia and corneal epithelial damage [6].

2.4. Conjunctivitis and oxidative stress

Whether it is infectious either it is bacterial, viral or non-infectious such as allergic conjunctivitis, oxidative stress is involved in its pathological process.

2.4.1. Infectious conjunctivitis

Pathogen invasion induces the aggregation of neutrophils, which produce a large amount of ROS through the respiratory burst. Although this can kill microorganisms, excessive release of ROS will damage adjacent ocular surface cells [7].

2.4.2. Allergic conjunctivitis

Allergens stimulate mast cells to release inflammatory mediators such as histamine, and at the same time activate NADPH oxidase, leading to the explosive production of ROS, which exacerbates conjunctival edema and pruritus [8].

2.5. Other ocular surface diseases

Diseases such as corneal epithelial injury and pterygium are also closely related to oxidative stress. For example, ultraviolet radiation can induce corneal epithelial cells to produce ROS, destroy intercellular junctions, and delay wound healing; in pterygium tissue, the activity of antioxidant enzymes, such as superoxide dismutase decreases, while the level of ROS increases, which promotes the abnormal proliferation of fibroblasts [9].

3. Antioxidant mechanism and ocular surface protection effect of hydrogen-rich water

3.1. Selective scavenging of toxic ROS

The core advantage of hydrogen-rich water lies in its selective antioxidant property: hydrogen molecules can penetrate cell membranes and specifically scavenge highly cytotoxic hydroxyl radicals (·OH) and peroxynitrite

($ONOO^-$), while having little impact on reactive oxygen species (ROS) with physiological functions, such as hydrogen peroxide, H_2O_2 [3]. In ocular surface tissues, this property can reduce the damage of oxidative stress to lacrimal gland cells and conjunctival epithelium. Animal experiments have shown that topical application of hydrogen-rich water can decrease the level of ·OH in the tear fluid of rats with dry eye syndrome and alleviate lipid peroxidation damage to the corneal epithelium [10].

3.2. Inhibition of inflammatory signaling pathways

Hydrogen-rich water exerts anti-inflammatory effects through multiple pathways.

(a) Downregulation of the NF-κB pathway. Hydrogen molecules inhibit the nuclear translocation of NF-κB, reduce the transcription of inflammatory factors such as tumor necrosis factor-α (TNF-α) and interleukin-1β (IL-1β), thereby alleviating ocular surface inflammatory responses [11].

(b) Regulation of the MAPK pathway: Hydrogen-rich water can inhibit the phosphorylation of kinases such as c-Jun N-terminal kinase (JNK) and p38 mitogen-activated protein kinase (p38 MAPK), blocking the transmission of inflammation signals induced by oxidative stress [12]. In a model of allergic conjunctivitis, eye drops containing hydrogen-rich water significantly reduced the expression of interleukin-6 (IL-6) and eosinophil chemokines in conjunctival tissues, and relieved conjunctival hyperemia and edema [13].

(c) Protection of ocular surface cell function: Promotion of cell survival: By activating the Nrf2/ARE (nuclear factor erythroid 2-related factor 2/antioxidant response element) antioxidant pathway, hydrogen-rich water upregulates the expression of antioxidant enzymes such as heme oxygenase-1 (HO-1) and glutathione peroxidase, enhancing the damage resistance of ocular surface cells [14].

(d) Delay of cell apoptosis: Hydrogen molecules can inhibit the decrease of mitochondrial membrane potential, reduce the release of cytochrome C, thereby suppressing the caspase-3-mediated apoptotic pathway and protecting lacrimal gland acinar cells and corneal epithelial cells [15].

3.3. Clinical evidence of hydrogen-rich water in improving ocular surface diseases

3.3.1. Clinical intervention for dry eye syndrome

A randomized controlled trial included 60 patients with mild to moderate dry eye syndrome, divided into the hydrogen-rich water eye drop group (twice a day, 1 drop each time, 4-week course) and the control group (normal saline).

The results showed that: The tear film break-up time (BUT) in the hydrogen-rich water group was prolonged by 2.3 ± 0.8 seconds compared with the baseline, which was significantly better than that in the control group (0.5 ± 0.3 seconds, $p < 0.05$); The Ocular Surface Disease Index (OSDI) score decreased by 12.5 ± 3.2 points in the hydrogen-rich water group, significantly superior to the control group (3.1 ± 1.5 points, $p < 0.05$); The improvement rate of patients' subjective symptoms such as dryness and burning sensation reached 85.3%, and no adverse reactions such as eye irritation occurred [16].

3.3.2. Improvement of ocular surface symptoms related to eye fatigue

Another study on people with eye fatigue showed that hydrogen-rich water eye drops (twice a day, 8-week course) could significantly improve the following indicators: The subjective scores of eye dryness and red blood streaks decreased by 62.7% and 58.9% respectively, which were significantly better than those in the control group; The uncorrected visual acuity increased by an average of 0.21 ± 0.05, and the myopia rate decreased from 15 to 5% (*p*

< 0.05); The patient satisfaction rate reached 95.5%, indicating that hydrogen-rich water has a positive intervention effect on ocular surface fatigue caused by long-term eye use [17].

3.3.3. Safety and tolerability

Multiple clinical studies have not found serious adverse reactions of hydrogen-rich water when applied to the ocular surface. Only a very small number of subjects experienced transient eye stinging (incidence < 3%), which may be related to the weak alkalinity of hydrogen-rich water (pH 13.5), but it can be relieved without special treatment [16,17]. Compared with the irritation of traditional antioxidants, such as vitamin C eye drops, hydrogen-rich water has more advantages in safety.

4. Research prospects

At present, the clinical application concentration (hydrogen solubility is usually 0.8–1.6 mg/L) and dosage form (simple aqueous solution) of hydrogen-rich water have not yet been unified. How to improve the residence time and bioavailability of hydrogen molecules on the ocular surface remains a challenge [18].

4.1. Unclear long-term effects

Most studies have an observation period of ≤ 8 weeks. The long-term efficacy of hydrogen-rich water on chronic ocular surface diseases such as severe dry eye and whether drug resistance exists need further verification [19]. In the future, exploring the combined application of hydrogen-rich water with artificial tears and anti-inflammatory drugs, such as the combination of hydrogen-rich water and 0.1% cyclosporine eye drops may regulate immunity while exerting antioxidant effects, thereby enhancing the therapeutic effect on dry eye [20].

4.2. Precision mechanism research

Using proteomics and metabolomics technologies to screen the key targets of hydrogen-rich water acting on the ocular surface, such as identifying hydrogen molecule-regulated oxidative stress-related microRNAs (e.g., miR-146a) [21].

4.3. Development of new formulations

Research and development of sustained-release formulations such as hydrogen-rich hydrogels and nano-emulsions to prolong the residence time on the ocular surface and improve antioxidant efficiency [22].

5. Conclusion

Oxidative stress plays a key role in the occurrence and development of ocular surface diseases. Hydrogen-rich water, through its selective antioxidant, anti-inflammatory, and cytoprotective effects, provides a new intervention approach for ocular surface diseases such as dry eye and asthenopia. Existing clinical evidence shows that hydrogen-rich water can significantly improve the oxidative stress state of the ocular surface, alleviate symptoms such as dryness and red blood streaks, and have high safety. In the future, it is necessary to further optimize the dosage form, clarify the long-term effects, and in-depth explore the value of its combined application with other therapies, so as to promote the wide application of hydrogen-rich water in the clinical prevention and treatment of

ocular surface diseases.

Disclosure statement

The author declares no conflict of interest.

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